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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/689,866	10/21/2003	Benjamin Oshlack	200.1133CON	3333

7590 04/07/2008  
DAVIDSON, DAVIDSON & KAPPEL, LLC  
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485 Seventh Avenue  
New York, NY 10018

EXAMINER
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SHEIKH, HUMERA N

ART UNIT	PAPER NUMBER
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1618

MAIL DATE	DELIVERY MODE
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04/07/2008

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/689,866	<b>Applicant(s)</b> OSHLACK ET AL.	
	<b>Examiner</b> Humera N. Sheikh	<b>Art Unit</b> 1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 26 December 2007.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-59 and 61 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-59 and 61 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                       | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>12/26/07; 3/21/08</u> .                                       | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### **Status of the Application**

Receipt of the Response after Non-Final Office Action, the Amendments and Applicant's Arguments/Remarks, all filed 12/26/07 and the Information Disclosure Statements (IDS) filed 12/26/07 and 03/21/08 is acknowledged.

Claims 1-59 and 61 are pending in this action. Claims 1-9, 29-32, 41 and 54 have been amended. Claim 60 has previously been cancelled. Claims 1-59 and 61 remain rejected.

### ***Claim Rejections - 35 USC § 103***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

**Claims 1-59 and 61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Palermo (WO 99/32120).**

**Palermo (WO '120)** teaches an oral dosage form of an opioid analgesic, comprising an analgesically effective amount of an opioid agonist together with an opioid antagonist, the amount of opioid antagonist including being sufficient to counteract opioid effects if extracted together with the opioid agonist (see p. 6, lines 1-18).

In certain preferred embodiments, the opioid agonist is hydrocodone, hydromorphone, oxycodone, morphine or pharmaceutically acceptable salts thereof (p. 7, lines 5-6). Suitable opioid antagonists disclosed include naltrexone, naloxone, nalmephene, cyclazocine and

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levallorphan. A most preferred antagonist is naltrexone (p. 11, lines 14-19); (p. 13, lines 14-31). In certain preferred embodiments of the method, the opioid agonist and the opioid antagonist are combined in a ratio of opioid antagonist to opioid agonist which is analgesically effective when the combination is administered orally, but which is aversive in a physically dependent subject (p. 7, lines 7-15). In embodiments where the opioid is hydrocodone and the antagonist is naltrexone, the ratio of naltrexone to hydrocodone is preferably from about 0.03-0.27:1 by weight (p. 7, lines 15-26).

Palermo teaches that the dosage forms of the invention may be liquids, tablets, multiparticulates, dispersible powders or granules, hard or soft capsules, lozenges, aqueous or oily suspensions, emulsions, syrups, elixirs, microparticles, buccal tablets, etc. (p. 7, lines 27-31); (p. 8, line 29 – p. 9, line 1). In certain preferred embodiments, the oral dosage forms are sustained release formulations. This may be accomplished via the incorporation of a sustained release carrier into a matrix containing the opioid agonist and opioid antagonist; or via a sustained release coating of a matrix containing the opioid agonist and opioid antagonist, where the sustained release coating contains at least a portion of the sustained release carrier included in the dosage form (p. 8, lines 1-9); (p. 20, lines 16-21).

With regards to ratios, Palermo teaches that the combinations of opioid antagonists/opioid agonists which are orally administered in ratios which are equivalent to the ratio of e.g., naltrexone to hydrocodone set forth are considered to be within the scope of the invention. For example, in some embodiments, naloxone is utilized as the opioid antagonist, the amount of naloxone included in the dosage form being large enough to provide an

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equiantagonistic effect as if naltrexone were included in the combination (p. 19-31). This demonstrates bioequivalency of the dosage forms.

Palermo teaches that the dosage forms may be coated with one or more materials suitable for the regulation of release or the protection of the formulation. The coatings are provided to permit either pH-dependent or pH-independent release (p.21, lines 18-29).

In preferred embodiments, the substrate (e.g., tablet core bead, matrix particle) containing the opioid analgesic is coated with a hydrophobic material selected from (i) an alkylcellulose; (ii) an acrylic polymer or (iii) mixtures thereof (p. 22, lines 6-14).

Suitable and preferred alkylcellulose polymers taught include ethylcellulose (p. 22, lines 19-25). Acrylic polymers are also disclosed and include acrylic acid and methacrylic acid copolymers, methyl methacrylate copolymers, ethoxyethyl methacrylates, cyanoethyl methacrylate, poly(acrylic acid), poly(methacrylic acid) and the like (p. 23, line 10 – p. 24, line 22); (p. 29, lines 7-18). Plasticizers can also be included in the composition (p. 24, line 24 – p. 25, line 20). A process for preparing coated beads is disclosed at p. 25, line 21 – p. 28, line 8. Matrix bead formulations are disclosed at page 28. Hydrophilic and/or hydrophobic materials, such as gums, cellulose ethers, acrylic resins, protein derived materials and any pharmaceutically acceptable hydrophobic material or hydrophilic material, which is capable of imparting, controlled release of the active agent and which melts (or softens to the extent necessary to be extruded) may be used in this invention (p. 28, lines 19-30).

With regards to the ratios, amounts and release rates claimed by Applicant, the Examiner notes that suitable or effective amounts, ratios or release rates of the agonist/antagonist can be determined by one of ordinary skill in the art through routine or manipulative experimentation to

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obtain optimal results as these are variable parameters attainable within the art. Moreover, generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. “[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.” *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

The Palermo reference explicitly recognizes and teaches oral dosage forms comprising opioid agonists and opioid antagonists, whereby the dosage forms are effective for the substantial reduction of pain. Given the teachings of Palermo discussed above, the instant invention, when taken as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

### ***Response to Arguments***

Applicant's arguments filed 12/26/07 have been fully considered but they are not persuasive.

#### **Rejection under 35 U.S.C. 103(a):**

Applicant argued, “The Palermo Publication describes dosage forms in which an opioid antagonist and an opioid agonist are combined in such a way that at least a two-step extraction process would be required to separate the opioid antagonist from the opioid agonist. The Palermo Publication does not teach or suggest ...particles of a therapeutically active agent consisting essentially of a sequestered opioid antagonist.”

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Applicant's arguments have been fully considered, but were not deemed persuasive. The "consisting essentially of" language does not exclude the presence of the additional therapeutic ingredient of the Palermo Publication. Applicant would further have the burden of showing that the formulation of the reference as a matrix would be detrimental to the results desired to be achieved. Given Applicant's disclosure at page 7, lines 20-31 and Claim 5 as instantly presented Applicant cannot distinguish from the matrix of the reference. The claimed embodiments would not exclude the matrix of the reference. Arguments based on rates of release are not supported by a showing of any unusual and/or unexpected results. The prior art teaches the same desired result. The arguments for the necessity of using a two-step extraction process for separation are not pertinent to the obviousness of the claimed formulation. Finally, note that the term "sequestered", even as defined by Applicant's specification, merely requires that the formulation at some point in time be non-releasable. For these reasons, the rejections of record have been maintained.

### ***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

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however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

--No claims are allowed at this time.

*Correspondence*

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Humera N. Sheikh whose telephone number is (571) 272-0604. The examiner can normally be reached on Monday, Tuesday, Thursday and Friday during regular business hours.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley, can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Humera N. Sheikh/

Primary Examiner, Art Unit 1618

*hns*

March 31, 2008



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